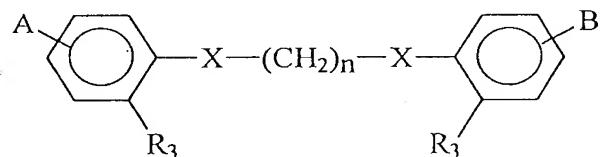


WE CLAIM:

1. A method of binding the imidazoline receptor, comprising:  
contacting a bis-benzene to said imidazoline receptor in an amount effective to  
5 bind to said receptor, wherein said bis-benzene contains at least one amidine group.
2. A method according to claim 1, wherein said contacting step is carried out  
*in vitro*.
- 10 3. A method according to claim 1, wherein said contacting step is carried out  
*in vitro* with cells that express said imidazoline receptor.
4. A method according to claim 1, wherein said contacting step is carried out  
*in vitro* with a cell-free preparation comprising said imidazoline receptor.  
15
5. A method according to claim 1, wherein said contacting step is carried out  
*in vivo*.
6. A method according to claim 1, wherein said contacting step is carried out  
20 *in vivo* by administering said compound to a subject afflicted with a disease state  
which is alleviable by treatment with a compound having high selectivity and affinity for  
the imidazoline receptor site.
7. A method according to claim 1, wherein said bis-benzene has the formula I:  
25

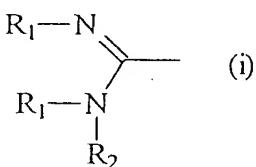


30

wherein:

A and B are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, nitro, amino, aminoalkyl, halo, hydroxy, carboxy, and compounds of formula (i):

5



10 subject to the proviso that at least one of A and B is a compound of formula (i);

R<sub>1</sub> and R<sub>2</sub> are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, alkoxyalkyl, cyloalkyl, aryl, hydroxyalkyl, aminoalkyl and alkylaminoalkyl; or two R<sub>1</sub> group on the same amidine group together represent -(CH<sub>2</sub>)<sub>m</sub>- wherein m is 2, 3, or 4;

15 R<sub>3</sub> is H, loweralkyl, oxyalkyl, alkoxyalkyl, hydroxyalkyl, cycloalkyl, aryl, aminoalkyl, alkylaminoalkyl or halogen;

n is from 2 to 6; and

X is O, NH, or S;

or a pharmaceutically acceptable salt thereof.

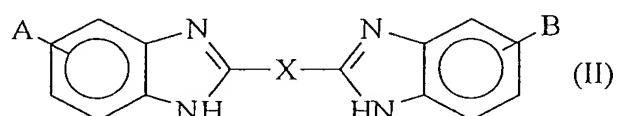
20

8. A method according to claim 7, wherein R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are H; wherein X is O; and wherein n is 5.

25

9. A method according to claim 1, wherein said bis-benzene has the formula

II:

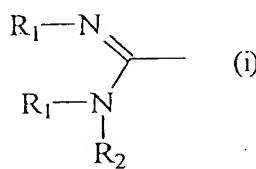


30

wherein:

A and B are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, nitro, amino, aminoalkyl, halo, hydroxy, carboxy, and compounds of formula (i):

5



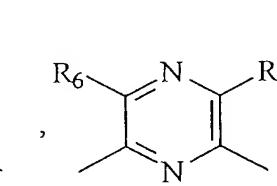
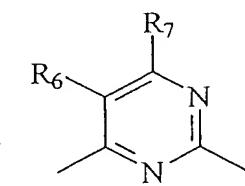
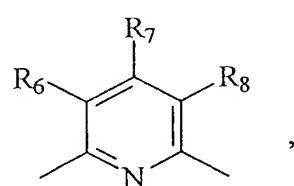
subject to the proviso that at least one of A and B is a compound of formula (i);

10 R<sub>1</sub> and R<sub>2</sub> are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, alkoxyalkyl, cyloalkyl, aryl, hydroxyalkyl, aminoalkyl and alkylaminoalkyl; or two R<sub>1</sub> group on the same amidine group together represent –(CH<sub>2</sub>)<sub>m</sub>– wherein m is 2, 3, or 4;

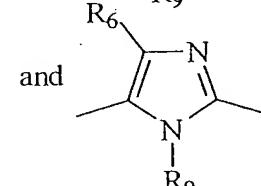
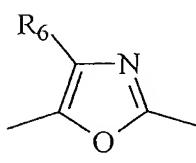
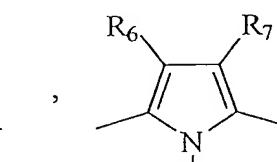
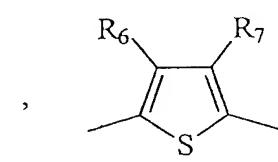
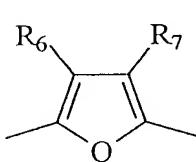
15 R<sub>3</sub> is H, loweralkyl, oxyalkyl, alkoxyalkyl, hydroxyalkyl, cycloalkyl, aryl, aminoalkyl, alkylaminoalkyl or halogen;

20 X is linear or branched, saturated or unsaturated C1-C12 alkyl containing up to 4 double bonds; or X is a heterocyclic aromatic group selected from the group consisting of:

25



30



30

wherein

R<sub>6</sub>, R<sub>7</sub>, and R<sub>8</sub> are each independently selected from the group consisting of H, loweralkyl, halogen, oxyalkyl, oxyaryl, or oxyarylalkyl;

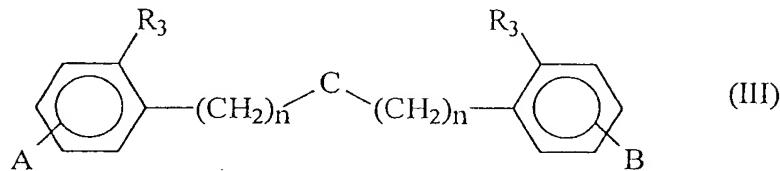
R<sub>9</sub> is hydrogen, loweralkyl, hydroxy, aminoalkyl or alkylaminoalkyl;

or the pharmaceutically acceptable salts thereof.

10. A method according to claim 1, wherein said bis-benzene has the formula

III:

5

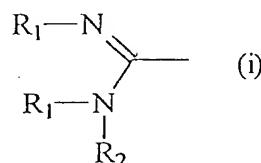


10

wherein:

A and B are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, nitro, amino, aminoalkyl, halo, hydroxy, carboxy, and substituents of formula (i):

15



20

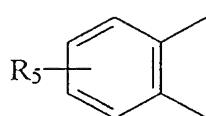
subject to the proviso that at least one of A and B is a substituent of formula (i);

R<sub>1</sub> and R<sub>2</sub> are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, alkoxyalkyl, cyloalkyl, aryl, hydroxyalkyl, aminoalkyl and alkylaminoalkyl; or two R<sub>1</sub> groups on the same amidine group together represent — (CH<sub>2</sub>)<sub>m</sub> — wherein m is 2, 3, or 4;

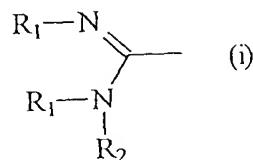
25 R<sub>3</sub> is H, loweralkyl, oxyalkyl, alkoxyalkyl, hydroxyalkyl, cycloalkyl, aryl, aminoalkyl, alkylaminoalkyl or halogen;

or two R<sub>1</sub> groups on the same amidine group together represent

30



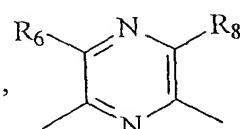
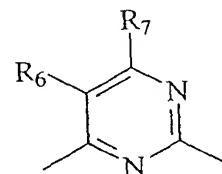
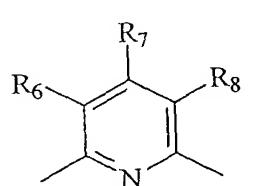
wherein  $R_5$  is



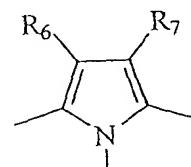
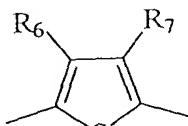
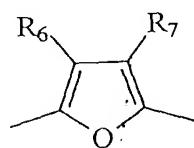
n is an integer from 0 to 2; and

A is a heterocyclic aromatic group selected from the group consisting of:

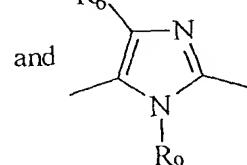
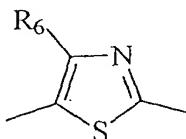
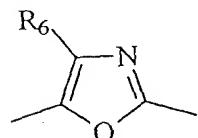
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15



20



wherein

25  $R_6$ ,  $R_7$ , and  $R_8$  are each independently selected from the group consisting of H,

loweralkyl, halogen, oxyalkyl, oxyaryl, or oxyarylalkyl;

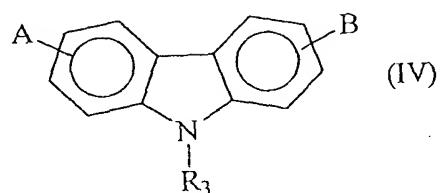
$R_9$  is hydrogen, loweralkyl, hydroxy, aminoalkyl or alkylaminoalkyl;

and the pharmaceutically acceptable salts thereof.

11. A method according to claim 1, wherein said bis-benzimidine has the

formula IV:

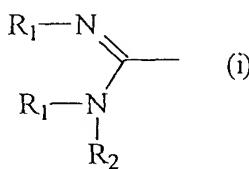
30



wherein:

A and B are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, nitro, amino, aminoalkyl, halo, hydroxy, carboxy, and substituents of formula (i):

5



subject to the proviso that at least one of A and B is a substituent of formula (i);

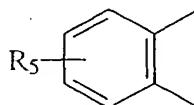
10

$\text{R}_1$  and  $\text{R}_2$  are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, alkoxyalkyl, cyloalkyl, aryl, hydroxyalkyl, aminoalkyl and alkylaminoalkyl; or two  $\text{R}_1$  group on the same amidine group together represent  $-(\text{CH}_2)_m-$  wherein m is 2, 3, or 4;

15

$\text{R}_3$  is H, loweralkyl, oxyalkyl, alkoxyalkyl, hydroxyalkyl, cycloalkyl, aryl, aminoalkyl, alkylaminoalkyl or halogen;

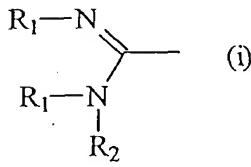
or two  $\text{R}_1$  groups on the same amidine group together represent



20

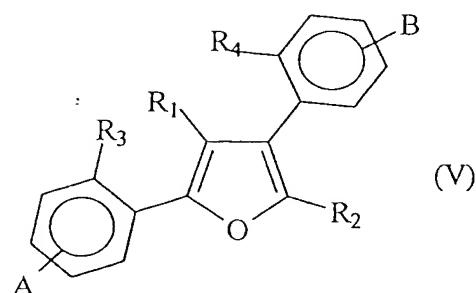
wherein  $\text{R}_5$  is

25



and the pharmaceutically acceptable salts thereof.

12. A method according to claim 1, said bis-benzene having the formula (V):

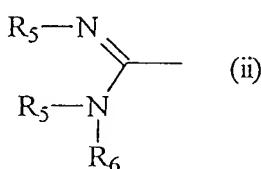


10

wherein:

A and B are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, nitro, amino, aminoalkyl, halo, hydroxy, carboxy, and substituents of formula (ii):

15



20

subject to the proviso that at least one of A and B is a substituent of formula (ii);

R<sub>1</sub> and R<sub>2</sub> are each independently selected from the group consisting of H, loweralkyl, aryl, alkylaryl, aminoalkyl, aminoaryl, halogen, oxyalkyl, oxyaryl, or oxyarylalkyl;

25 R<sub>3</sub> and R<sub>4</sub> are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, alkylaryl, aryl, oxyaryl, aminoalkyl, aminoaryl, or halogen; and

each R<sub>5</sub> is independently selected from the group consisting of H, loweralkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, cycloalkyl, aryl, or alkylaryl or two R<sub>5</sub> groups together represent C<sub>2</sub> to C<sub>10</sub> alkyl, hydroxyalkyl, or alkylene; and

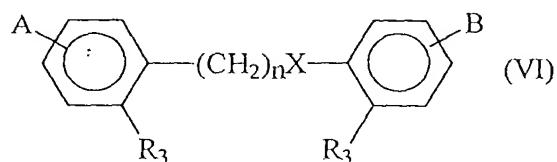
30 R<sub>6</sub> is H, hydroxy, loweralkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylamino, alkylaminoalkyl, cycloalkyl, hydroxycycloalkyl, alkoxycycloalkyl, aryl, or alkylaryl;

or a pharmaceutically acceptable salt thereof.

{

13. A method according to claim 1, wherein said bis-benzene has the formula VI:

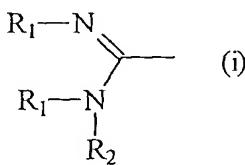
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wherein:

10 A and B are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, nitro, amino, aminoalkyl, halo, hydroxy, carboxy, and substituents of formula (i):

15

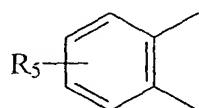


subject to the proviso that at least one of A and B is a substituent of formula (i);

20 R1 and R2 are each independently selected from the group consisting of H, loweralkyl, oxyalkyl, alkoxyalkyl, cyloalkyl, aryl, hydroxyalkyl, aminoalkyl and alkylaminoalkyl; or two R1 group on the same amidine group together represent -(CH2)m- where m is 2, 3, or 4;

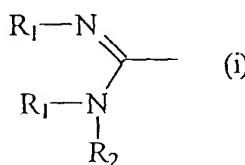
R3 is H, loweralkyl, oxyalkyl, alkoxyalkyl, hydroxyalkyl, cycloalkyl, aryl, aminoalkyl, alkylaminoalkyl or halogen;

25



wherein R5 is

30



X is O, S or NH;

n is an integer from 1 to 8;

and the pharmaceutically acceptable salts thereof.

5 14. A method of identifying imidazoline receptor binding agents, comprising  
the steps of:

providing a library of bis-benzene compounds, said bis-benzene compound  
containing at least one amidine group; and

screening said library for compounds that bind to said imidazoline receptor.

10

15. A method according to claim 14, wherein said library is a combinatorial  
library.

16. A method according to claim 14, wherein said bis-benzene compounds are  
15 immobilized on a solid support.

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